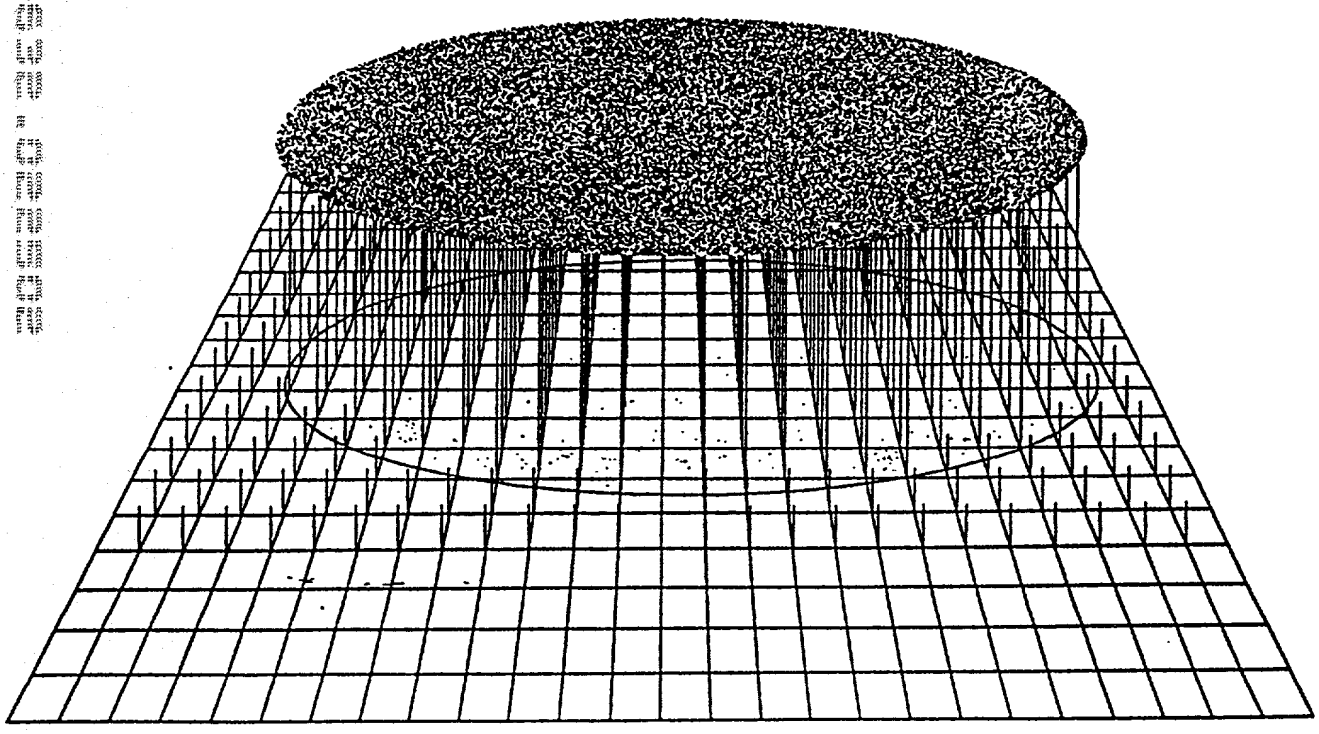
Aggregate vs. Scanning Ellipsometry

Innovation Group

Standard Immunoassay Use

Determination of mass per unit volume (eg. ng/ml) or equivalent (eg. IU)



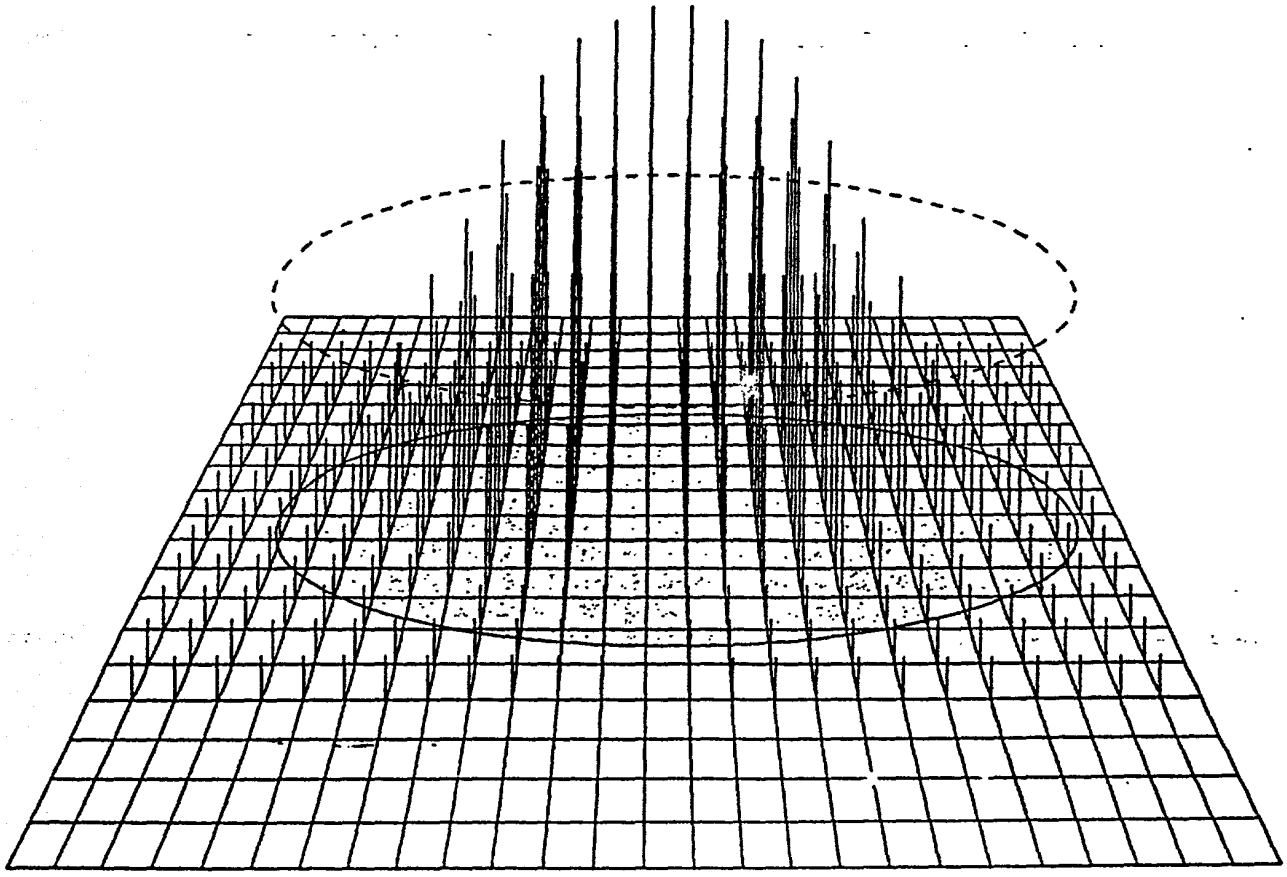
The effect of the use of a single large beam (in this case approx. 2mm) for reading the surface is the production of a single result representing the mass change effects of all binding events within the spot area.

Figure 1

Aggregate vs. Scanning Ellipsometry

Standard Immunoassay Use

Determination of mass per unit volume (eg. ng/ml) or equivalent (eg. IU)



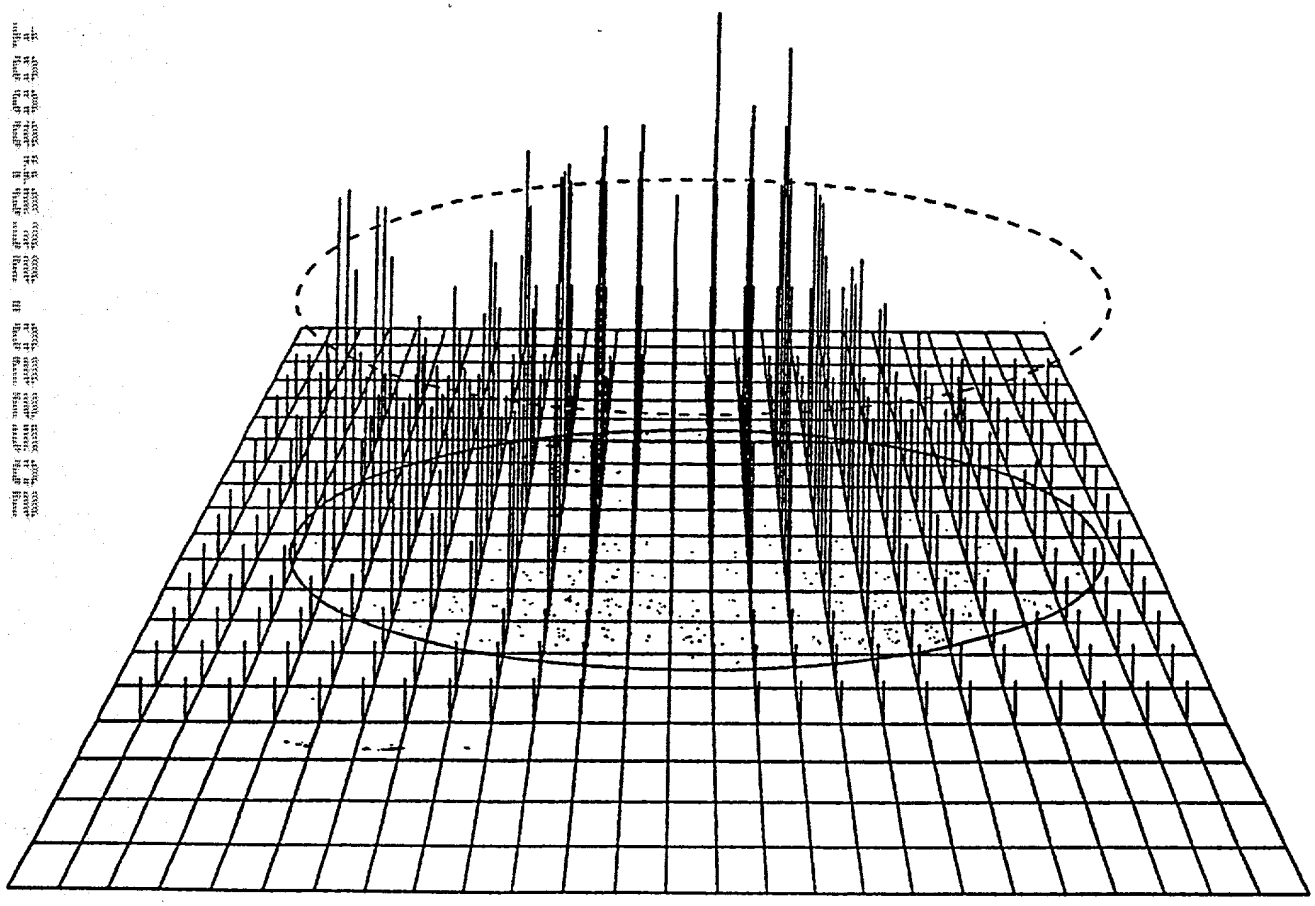
The idealized model for this method is the optical averaging occuring over the entire read area (in this case represented by an approx. normal distribution of binding events over the spot area).

Figure 2

Aggregate vs. Scanning Ellipsometry

Standard Immunoassay Use

Determination of mass per unit volume (eg. ng/ml) or equivalent (eg. IU)



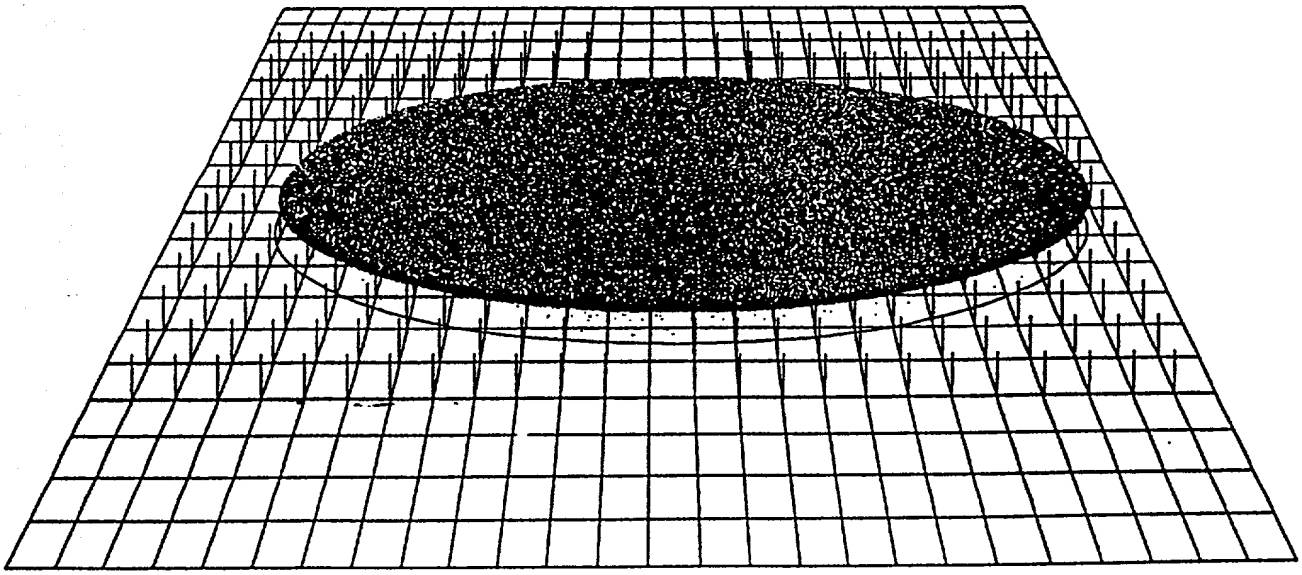
In virtually all cases the binding distribution over the spot area is actually highly inhomogenious. The advantage of this method is that it inherently integrates all of the binding events within the spot area, without regard to their distribution.

Figure 3

Aggregate vs. Scanning Ellipsometry

Standard Immunoassay Use

- Determination of mass per unit volume (eg. ng/ml) or equivalent (eg. IU)



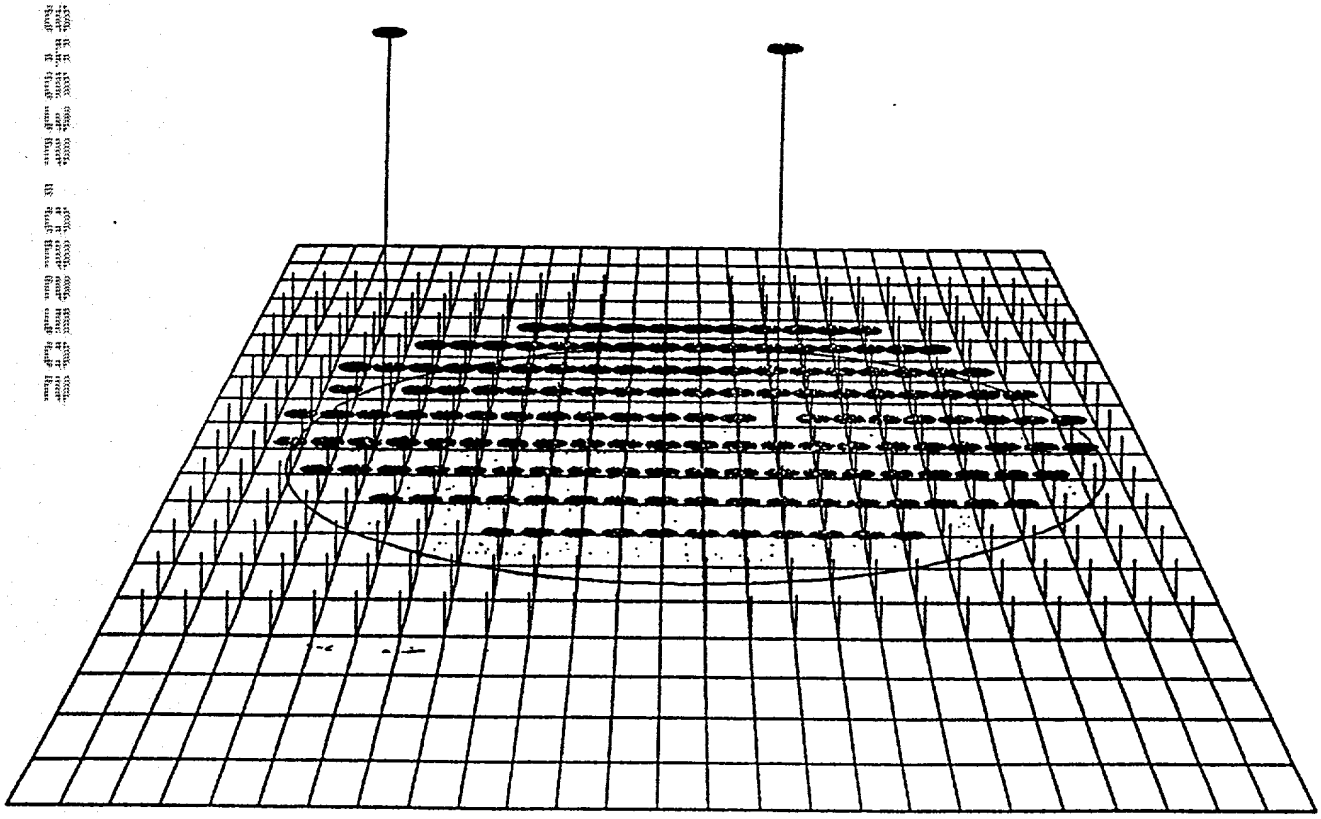
The disadvantage is that very small or very sparce binding events tend to be statistically reduced to insignificance when averaged over this relatively large spot area.

Figure 4

Aggregate vs. Scanning Ellipsometry

New Microbiological Use

Determination of individual binding events or CFUs



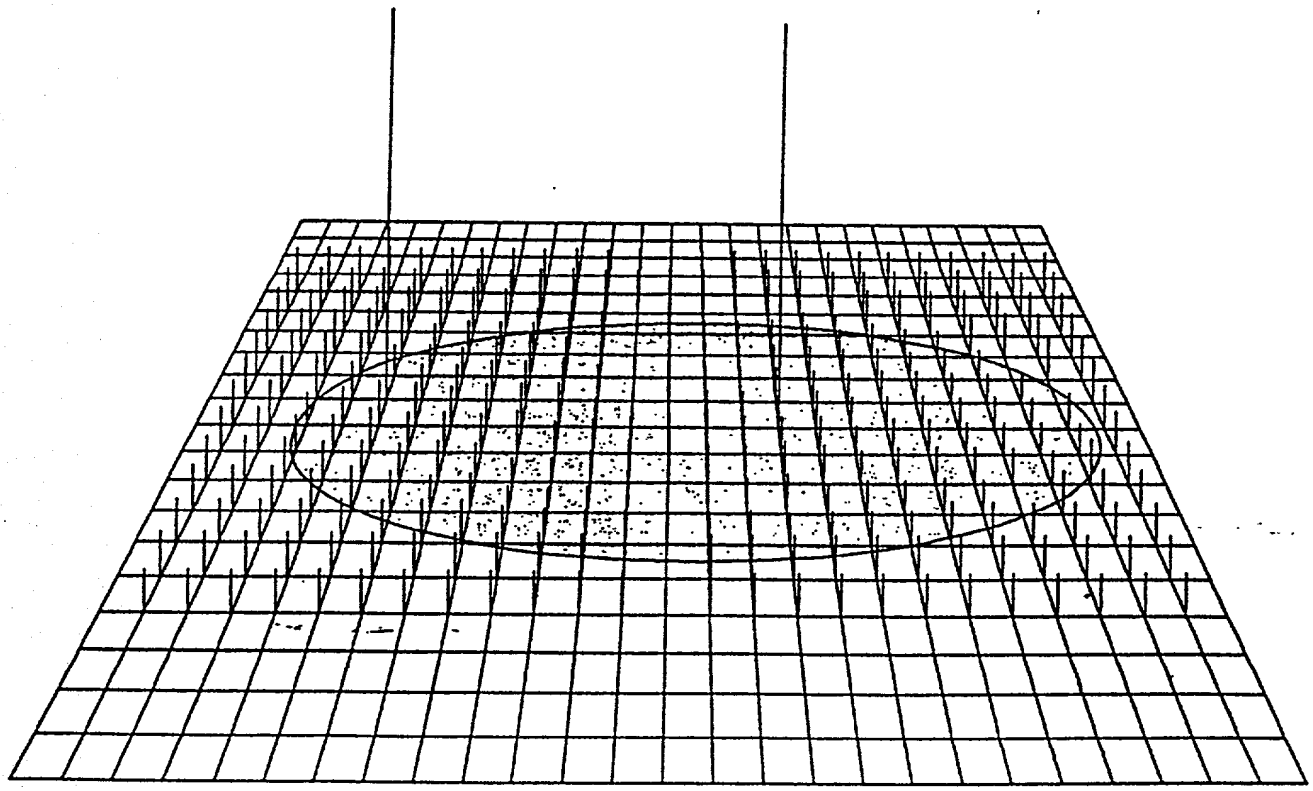
A scanning ellipsometric method or scatterometric method or both, when used with a very small beam diameter (in this case 20um) can provide a vastly higher relative signal for discreet binding events (that is as averaged over a much smaller spot area).

Figure 5

Aggregate vs. Scanning Ellipsometry

New Microbiological Use

Determination of individual binding events or CFUs

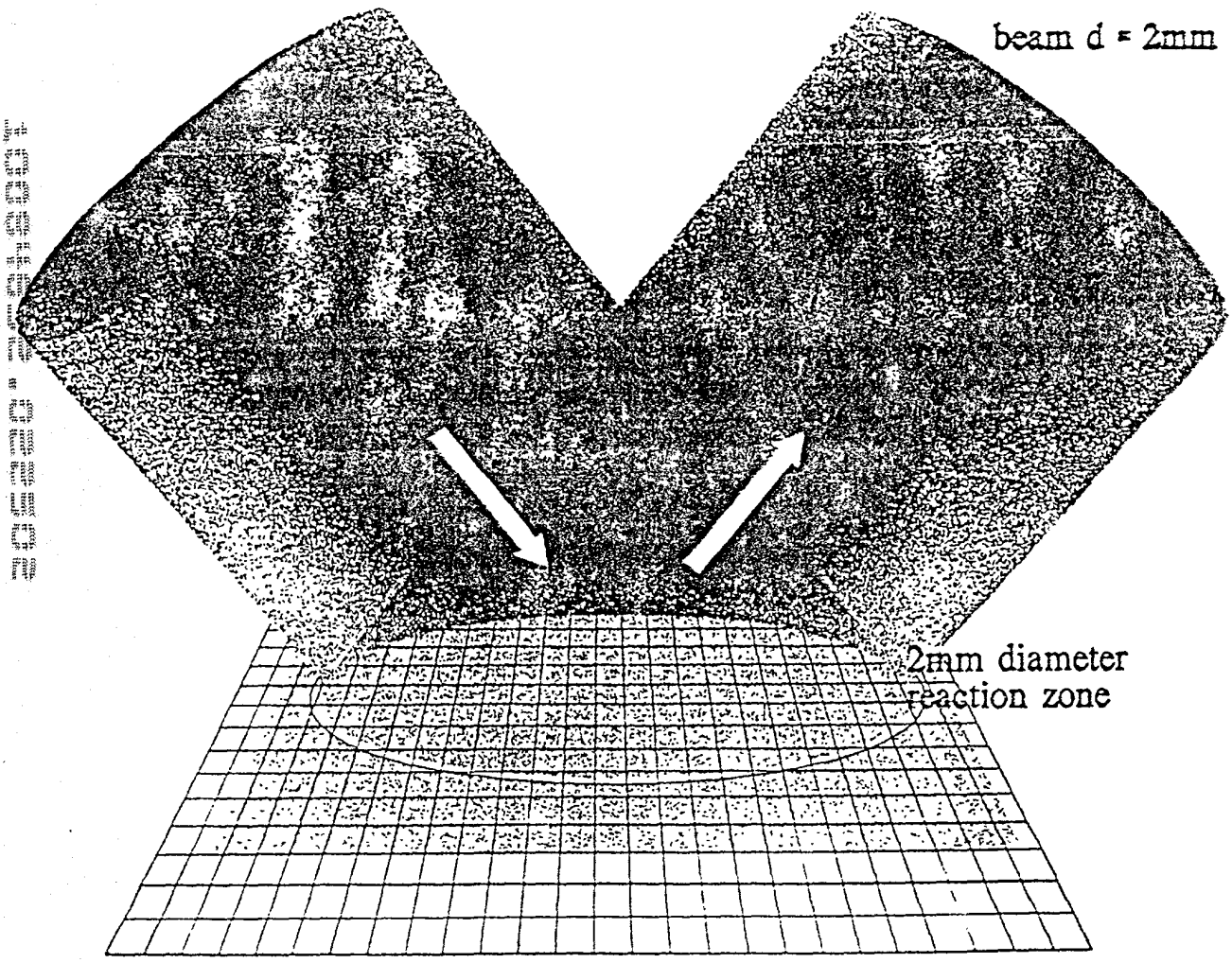


This approach allows for the surface to be ~~tracked~~ resolved as a type of topology. It is, in fact, because the binding events are not integrated over the surface that this method can be used to approximate individual or discreet binding event identification (depending upon the diameter of the beam used).

Figure 5

Aggregate vs. Scanning Ellipsometry

Current OTER Laser Configuration
Determination of aggregate response over the beam spot area



$pi \cdot r^2$ = SA (in mm^2) = 3.14159 x 1^2 = 3.14159 mm^2

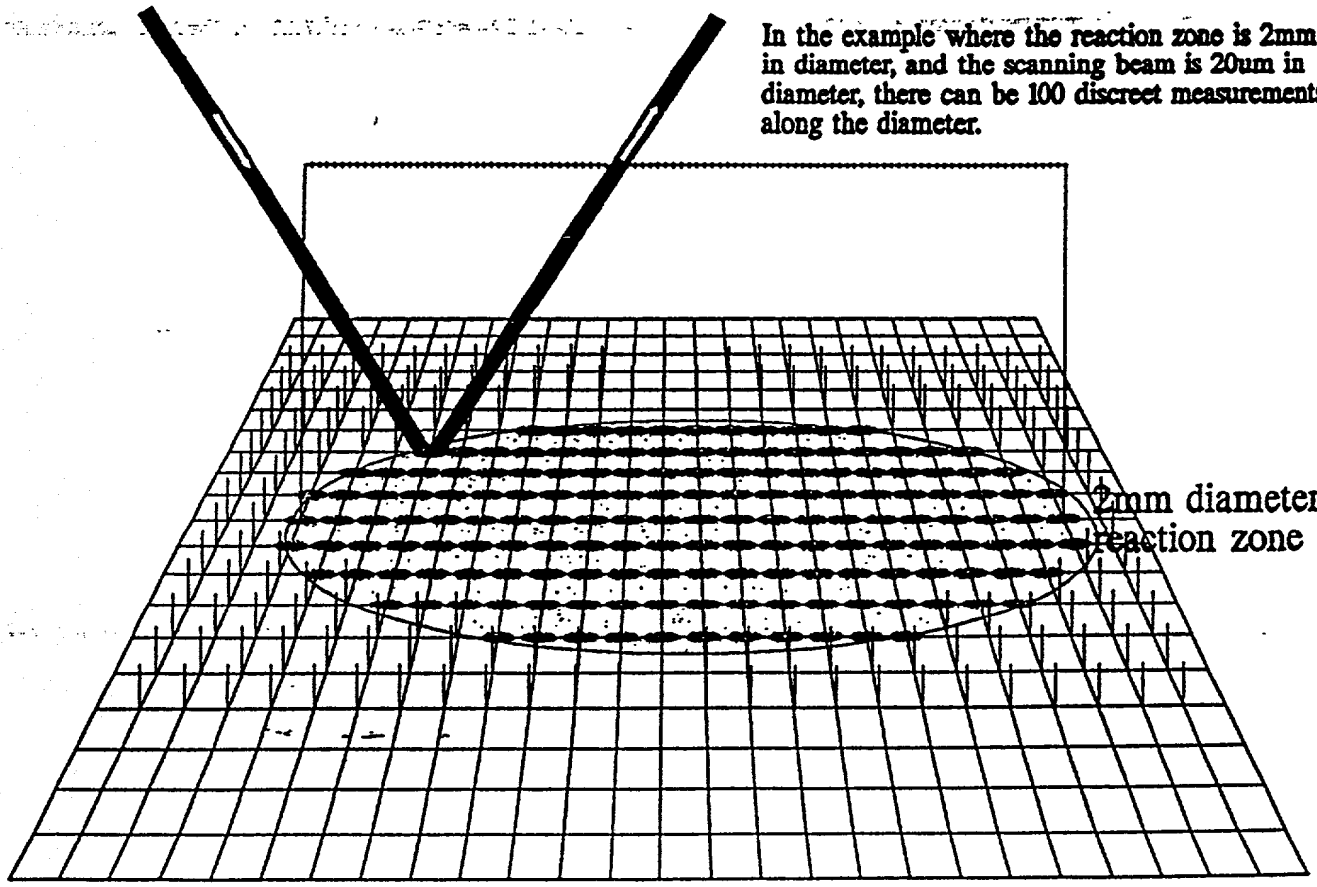
Figure 7

Aggregate vs. Scanning Ellipsometry

Scanning Micro-Laser Configuration
Determination of individual cellular-scale readings

For Example:
beam d = 20um

In the example where the reaction zone is 2mm in diameter, and the scanning beam is 20um in diameter, there can be 100 discreet measurements along the diameter.



10,000 A = 1um
1,000um = 1mm
Angstrom Unit = 3.937x10^-9 inch, 1x10^-10 meters, 1x10^-4, microns, 0.1 milli-micron (micro-millimeter).
Micron = 3.937x10^-5 inch, 0.039370 mil, 1x10^-6 meter, 0.001 millimeter, 1x10^4 Angstrom units.

1 mm^2 = 1,000,000 um^2 Reaction zone SA = 3,141,590 um^2 Scanning beam reads 314.159 um^2

Thus a 20um beam can make 10,000 discreet readings within the reaction zone

Figure 8

Aggregate vs. Scanning Ellipsometry

How Big is Small ?

In the case where a single organism (1 um^3) is to be measured on a 2 mm^2 surface:

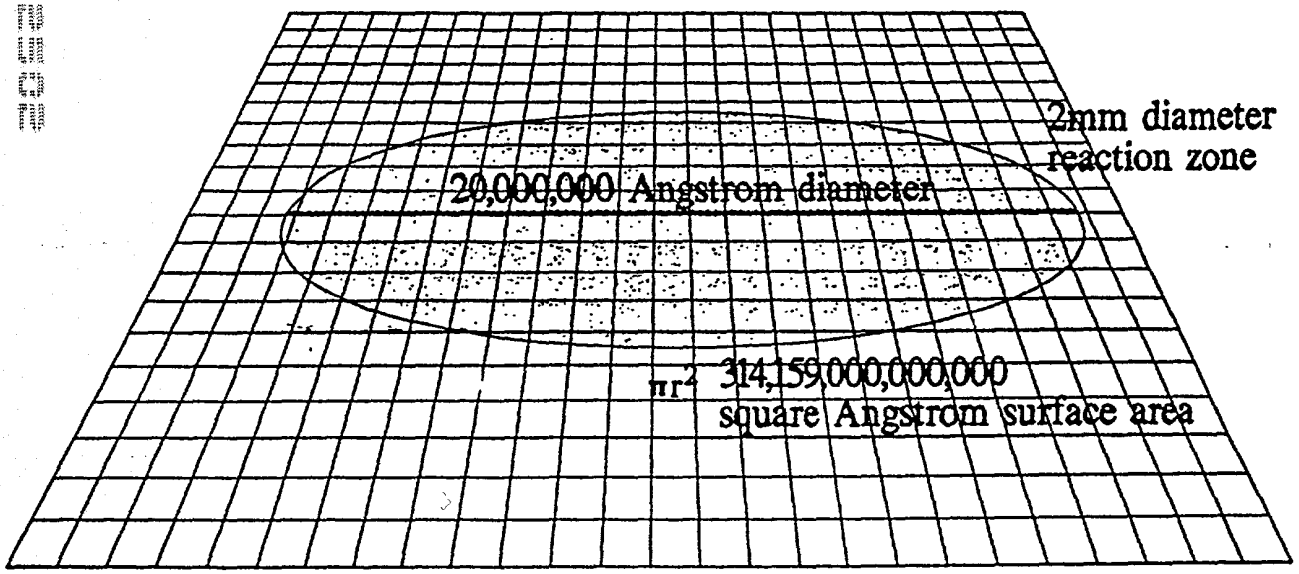
314,159,000,000,000 A^2 surface area of spot
78,500,000 A^2 surface area of organism ➡ ratio of 4,000,000 A^2 : 1 A^2

10,000 A (height) / 4,000,000 =.00250 A (height) contribution across the spot

1×10^2 cells / .02ml = 5×10^3 cells / ml ➡ .25 A (height) contribution across the spot
1×10^3 cells / .02ml = 5×10^4 cells / ml ➡ 2.5 A (height) contribution across the spot
1×10^4 cells / .02ml = 5×10^5 cells / ml ➡ 25 A (height) contribution across the spot
1×10^5 cells / .02ml = 5×10^6 cells / ml ➡ 250 A (height) contribution across the spot
1×10^6 cells / .02ml = 5×10^7 cells / ml ➡ 2500 A (height) contribution across the spot

probable unamplified detectability limit

With an amplification system that provided 2X mass, the system needs 2.5×10^6 cells / ml
With an amplification system that provided 5X mass, the system needs 1×10^6 cells / ml
With an amplification system that provided 10X mass, the system needs 5×10^5 cells / ml



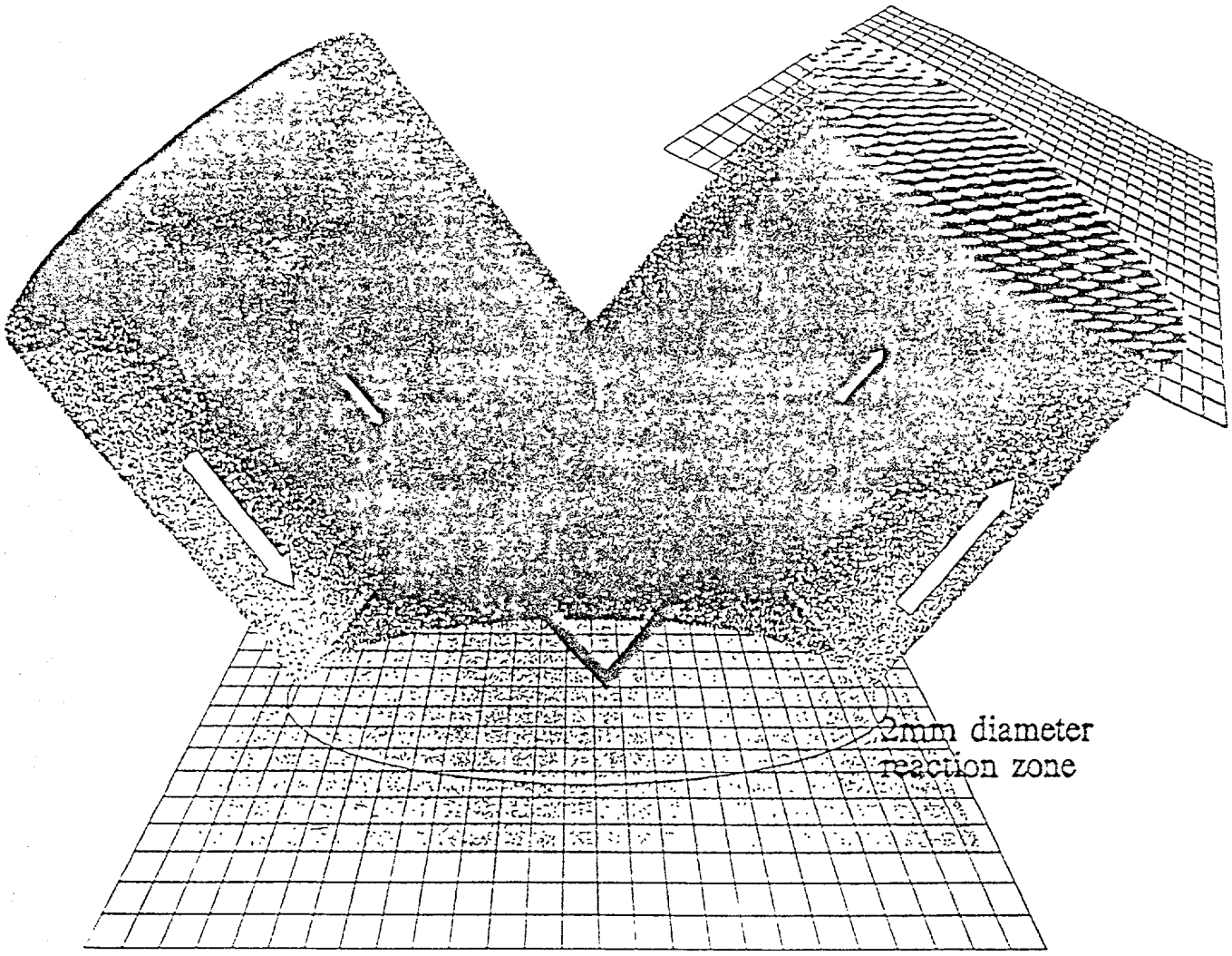
10,000 A = 1um
1,000um = 1mm
Angstrom Unit = 3.937x10^-9 inch, 1x10^-10 meters, 1x10^-4, microns, 0.1 milli-micron (micro-millimeter).
Micron = 3.937x10^-5 inch, 0.039370 mil, 1x10^-6 meter, 0.001 millimeter, 1x10^4 Angstrom units.

Figure 9

Scanning vs. Array Ellipsometry

An alternative to the small beam "Scanning" approach is the use of a CCD or diode array to read and "parce" the larger laser beam into smaller discreet signals.

Determination of small spot response within the large beam spot area



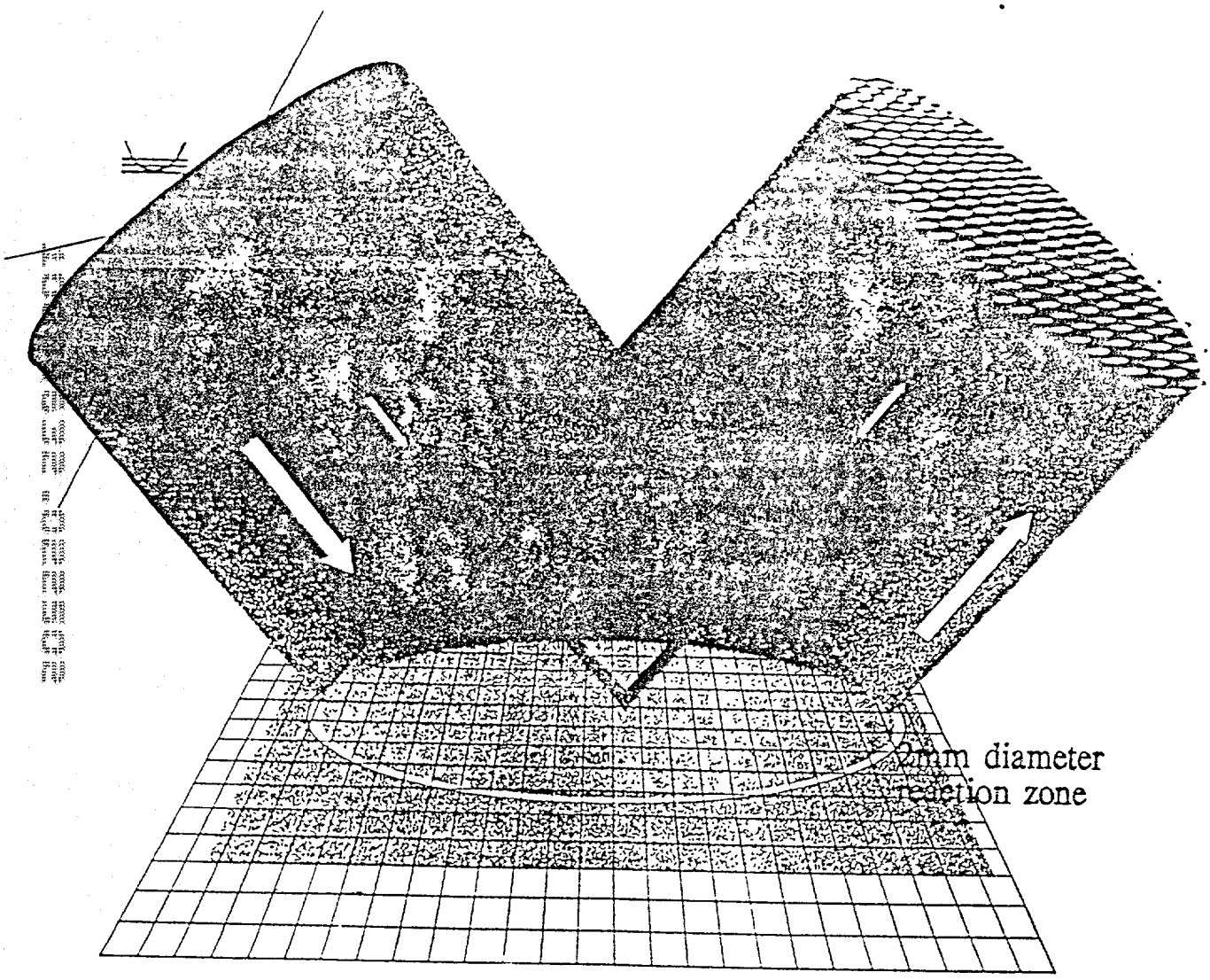
This effectively creates a "virtual" beam (defined by the path that the light intersecting the array at a specific dection point has taken).

The aggregate signal for all virtual beams equals the large beam signal, but each virtual beam references only a limited surface area. The virtual beam approach may be subject to greater error than the small beam approach, due in part to the potential for signal mixing across the array, however it allows for a major increase in sensitivity over the large beam approach.

Figure 10

Various Optical Signal Formats

The specific optical signal can be selected so as to provide the appropriate level of information, based upon the nature or the material to be detected, and the resolution desired.



A variety of optical signals may be used within this system.

The examples provided in this discussion use ellipsometry as the example optical method. However it is expected that a variety of optical methods will be substantially improved by adopting the general approach described here. In particular we have demonstrated that scattering methods will form the basis of one class of instruments that is distinct from ellipsometry. Other effects such as absorption, refractive index change, chiral effects, and diffraction may be used within an essentially similar optical configuration, and may provide particular and significant benefits.

Figure 11

Examples of Optical Signal Formats

Innovation Group

Principle	Label Type	Instrument	DDx Status
Scatter	polymer beads/particles silica beads/particles magnetic beads/particles metal beads/particles metal coated beads/particles	scatterometry	demonstrated
Optical absorption	colloidal gold magnetic beads	reflectometry photometry	scheduled
Change in polarization state	polymer beads silica beads	ellipsometry (with compensator) polarimetry (wout compensator)	scheduled
Change in refractive index	high refractive index or optically active materials	ellipsometry (with compensator) polarimetry (wout compensator)	scheduled
Chiral effects	azio dyes chiral compounds		envisioned
Diffraction effects	patterned surface	interferometry	envisioned
Spectroscopic effects	wavelength selective materials	spectrometer	envisioned

Signal reception techniques might include:

single diode detector - e.g. scanning (small beam method)
diode array detector - e.g. array (virtual beam method)
CCD detector - e.g. array (virtual beam method)

Figure 12

Potential for Optical Enhancement

For either the Scanning (small beam) or the Array (virtual beam) approach, a substantial improvement in signal delectability may be possible by using unique characteristics of optically based mass detection systems.

Properties of the mass enhancement label may alter the optical signal due to a number of physical characteristics, including:

- refractive index
- scatter
- chiral effect
- general adsorption
- wavelength specific adsorption
- diffraction

should be absorbance
What's the difference between these two?

effectively creating an improved ability to discriminate the signal generated by the binding of the label to the complex from that created by surface background or in the absence of specific binding events. This may operate through the creation of an enhanced or attenuated "apparent" signal over that which would be created by "normal" materials.

Scale of normal vs. optically active elements @ 2X effect

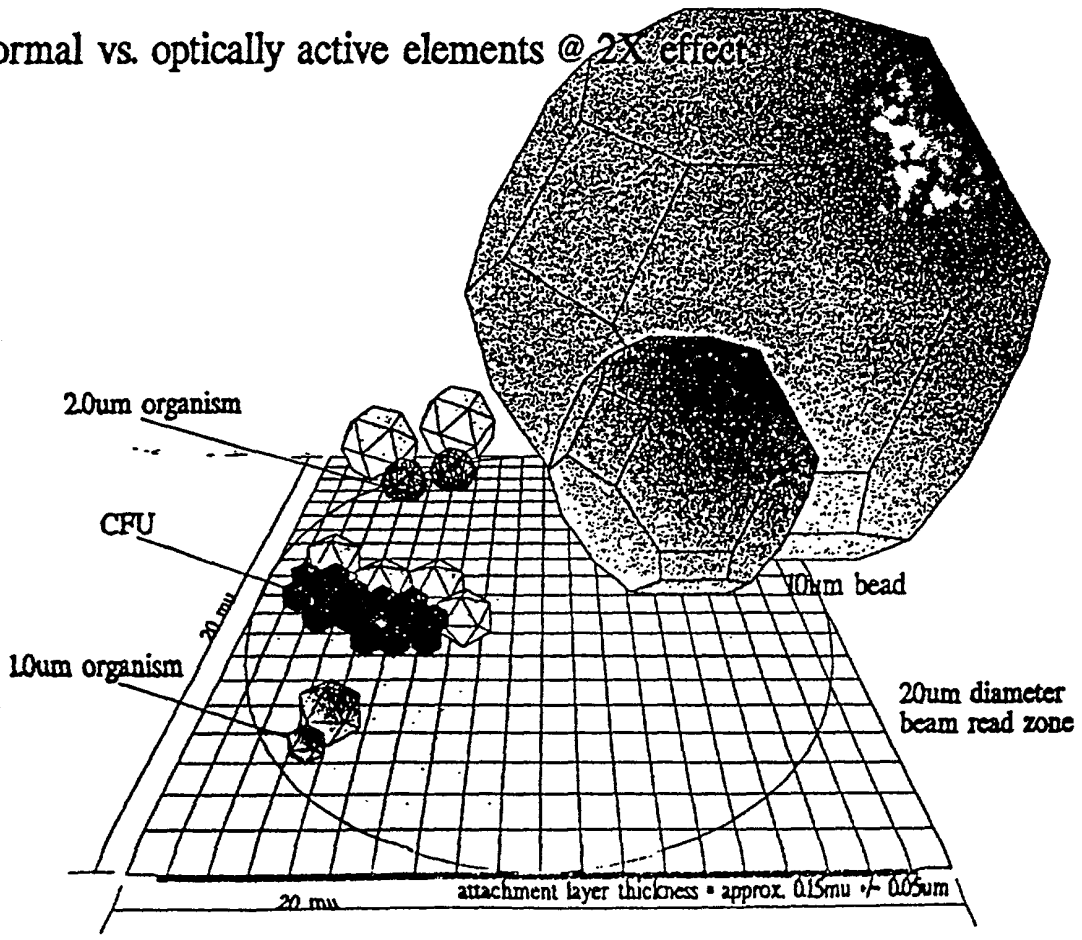


Figure 14

15/15

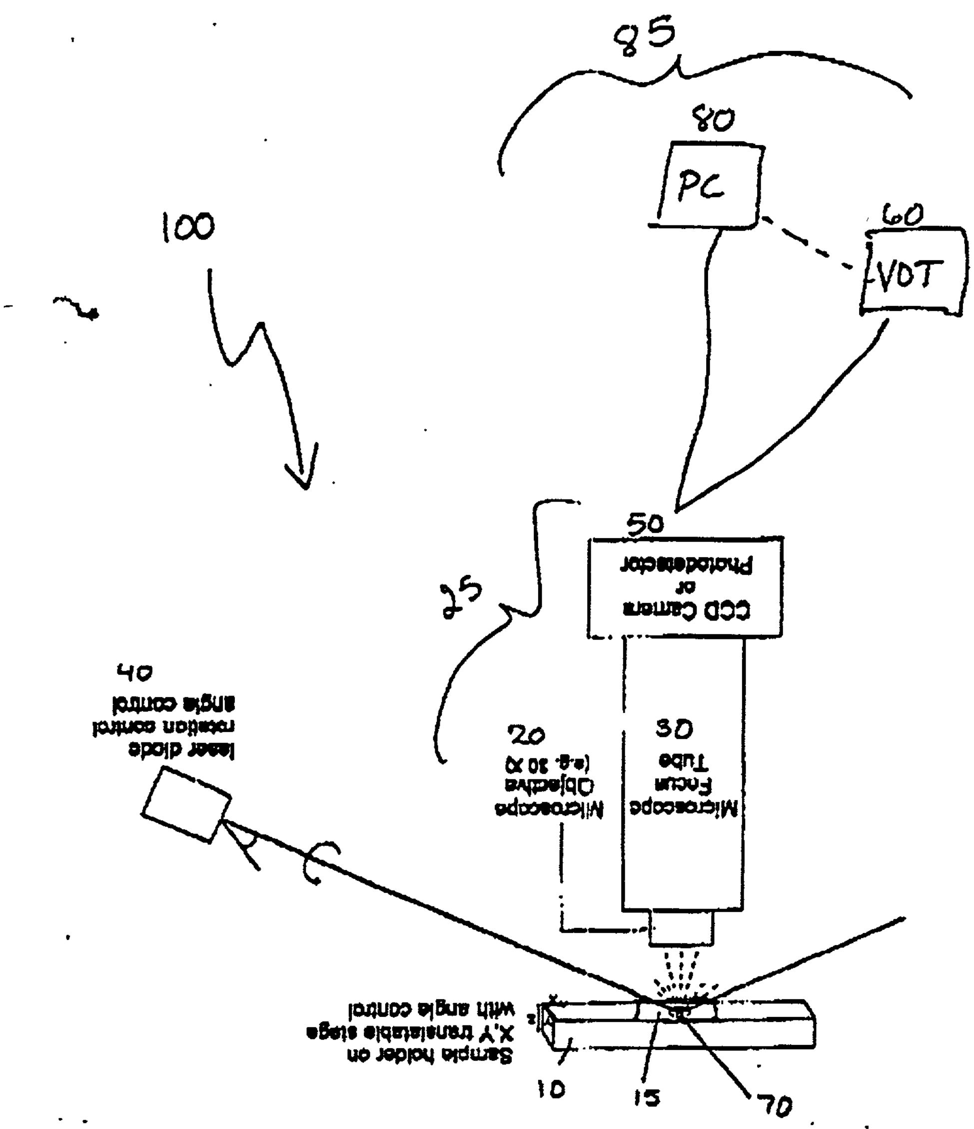

85
80
PC
60
VDT
100
50
CCD Camera
or
Photodetector
25
40
laser diode
rotation control
angle control
20
Microscope
Objective
(e.g. 30 X)
30
Microscope
Focus
Tube
Sample holder on
X,Y translatable stage
with angle control
10
15
70

Fig.15

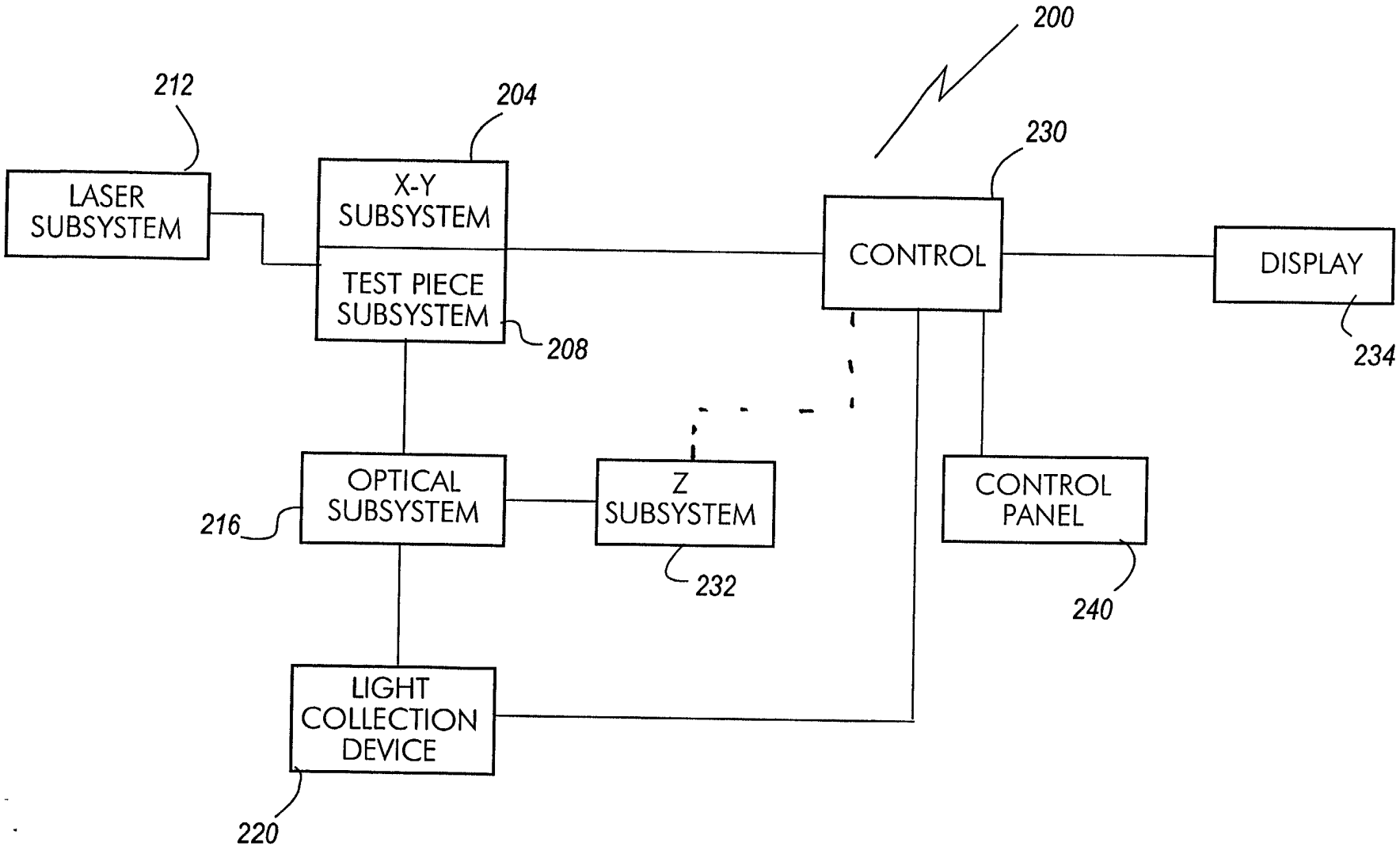

200
212
204
230
LASER SUBSYSTEM
X-Y SUBSYSTEM
TEST PIECE SUBSYSTEM
208
CONTROL
DISPLAY
234
OPTICAL SUBSYSTEM
216
Z SUBSYSTEM
232
CONTROL PANEL
240
LIGHT COLLECTION DEVICE
220

FIG. 16

GOOGLE PATENT

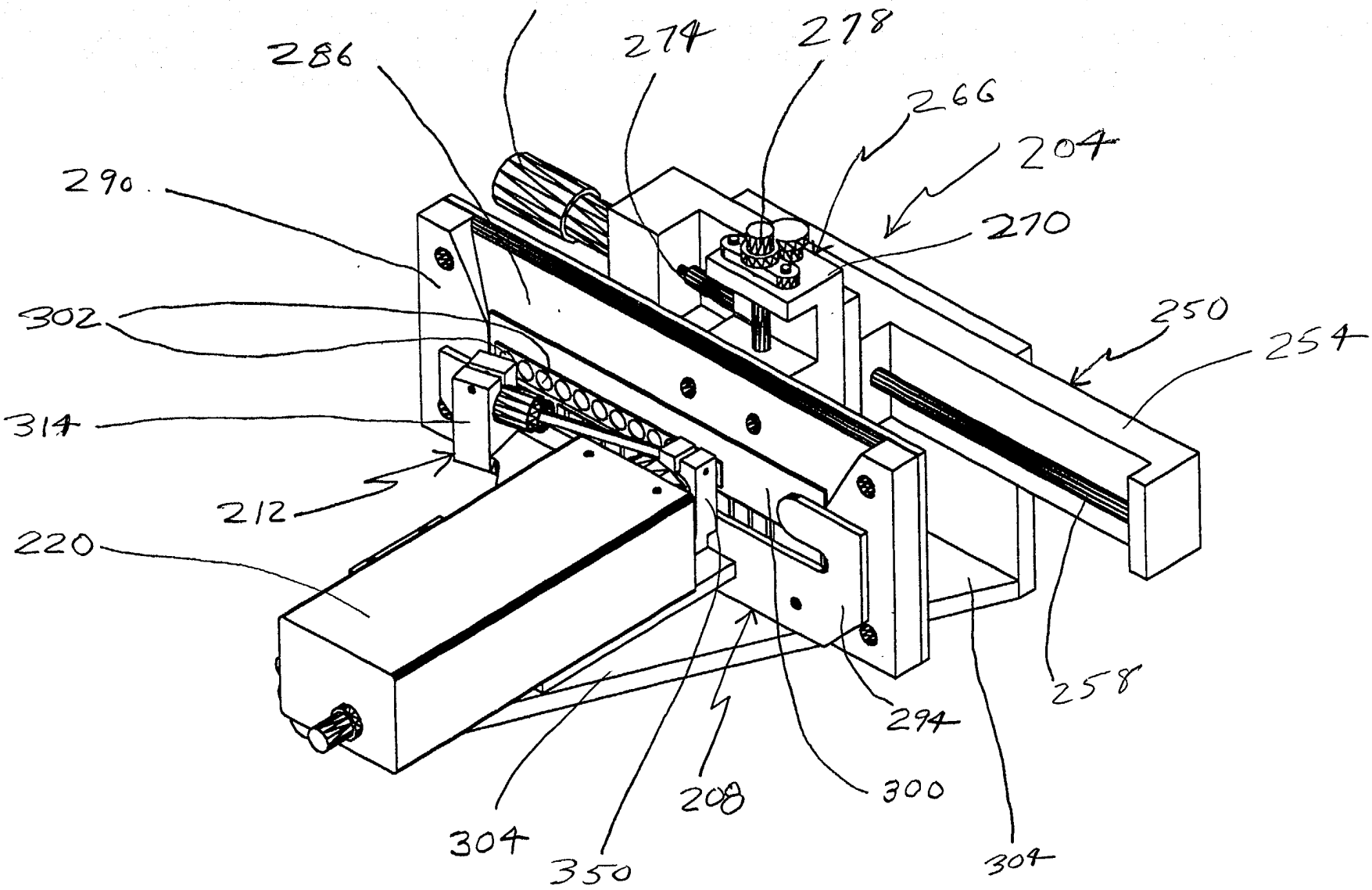


Fig. 17

NOTES: UNLESS OTHERWISE SPECIFIED

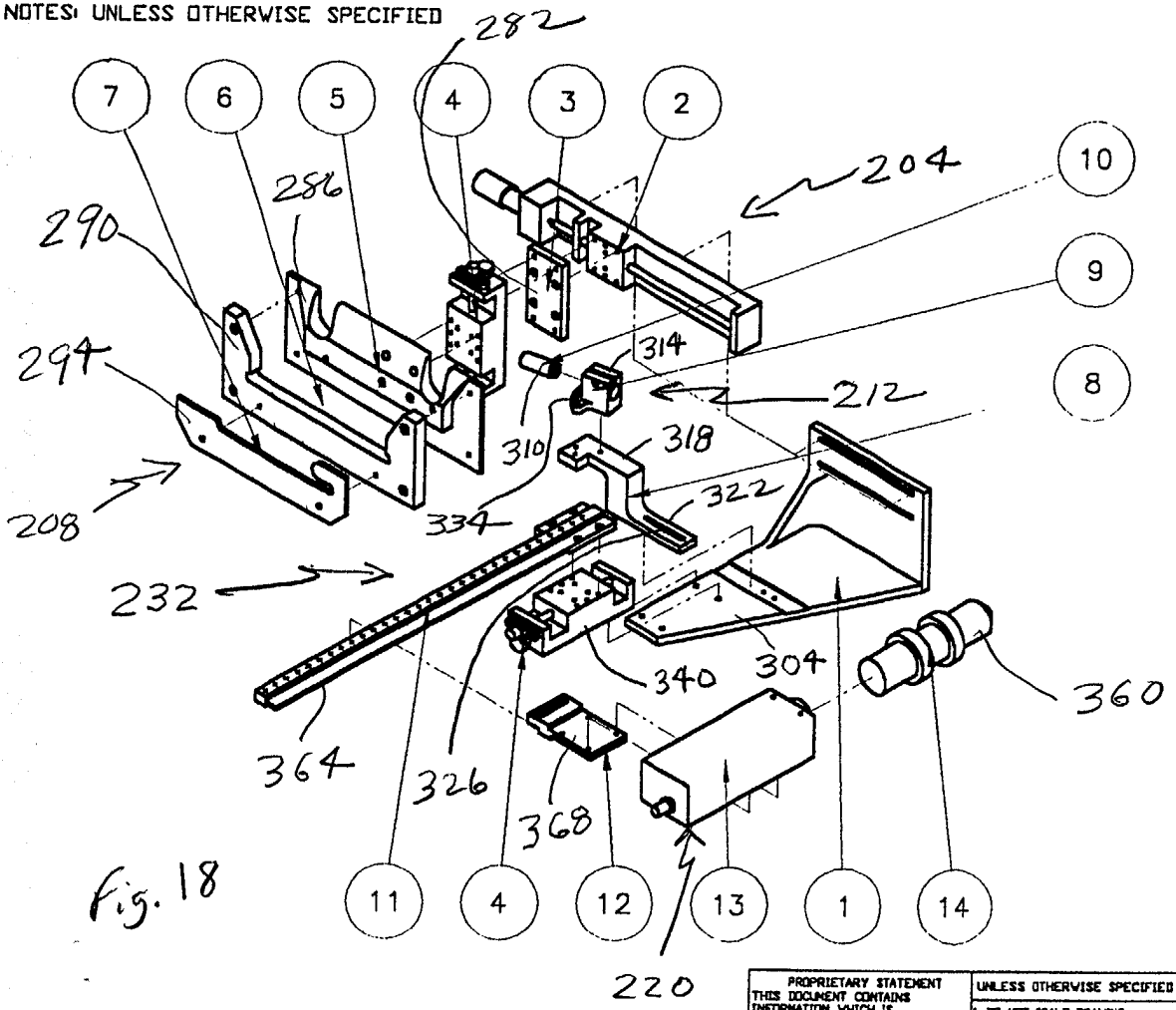


Fig. 18

REVISIONS				
ZONE	REV	DESCRIPTION	DATE	APPROVED
-	-	-	-	-

Item	Qty	PART
14	1	OBJECTIVE
13	1	CAMERA
12	1	CAMERA PLATE
11	1	Z PLATE
10	1	LASER
9	1	LASER HOLDER
8	1	LASER SUPPORT
7	1	TEST PIECE TOP
6	1	TEST PIECE SIDE
5	1	TEST PIECE BASE
4	2	MM-4M-F-25
3	1	X-Y PLATE
2	1	MM-4M-EX-108
1	1	BASE PLATE

Parts List

PROPRIETARY STATEMENT
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1. DO NOT SCALE DRAWING.
2. INTERPRET PER ANSI STANDARDS
3. DIMENSIONS APPLY PRIOR TO FINISH
4. DIMENSIONS ARE IN MILLIMETERS FOLLOWED BY (INCHES).
5. TOLERANCES ARE
.X (X.XX) = ± .5 (.02)
.XX (X.XXX) = ± .13 (.005)
.XXX (X.XXXX) = ± .013 (.0005)
X.X° = ± .25

DRAWN BY: JKO — DATE: 01-JUL-09
CHECKED: -
APPROVED: -
APPROVED: -

REFERENCE DOCUMENTS
REF
REF
REF

Scintilla
4901 W. 93rd Av. Apt 2232
Westminster, CO 80031
(303) 557-2859

TITLE: DDX ILLUMINATOR SYSTEM ASSEMBLY DRAWING

SIZE: B | TYPE: MACH | DWG. NO. | REV: 2
SCALE: 1/X | CONTRACT | SHEET 1 OF 1

CONFIDENTIAL

NOTES: UNLESS OTHERWISE SPECIFIED

REVISIONS				
ZONE	REV	DESCRIPTION	DATE	APPROVED
-	-	-	-	-

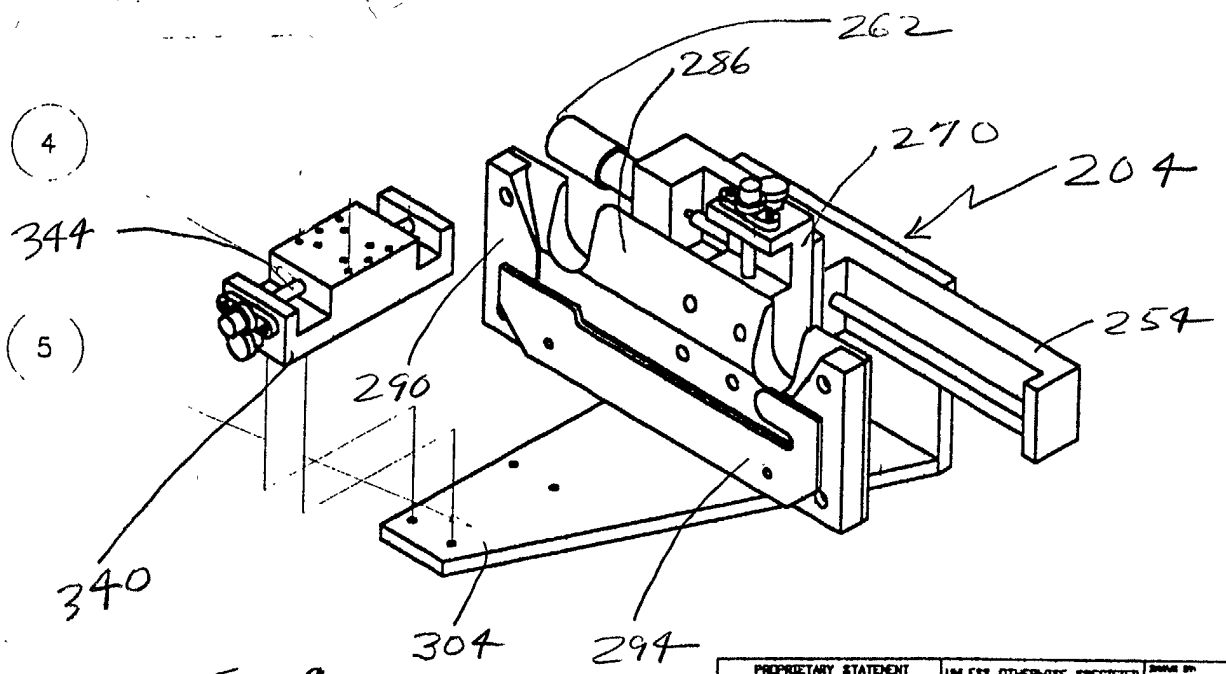

Fig. 19

Item	Qty	Name
5	5	FORTH ASSEMBLY
4	4	MM-4M-F-25
3	3	Z-PLATE
2	2	LENS CELL HOLDER
1	1	LASER HOLDER

Parts List

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4. DIMENSIONS ARE IN MILLIMETERS FOLLOWED BY (INCHES).
5. TOLERANCES ARE:
.X (X.XX) = ± .5 (.02)
.XX (X.XXX) = ± .13 (.005)
.XXX (X.XXXX) = ± .013 (.0005)
X.X° = ± .25

DRAWN BY	JKD	DATE 04-JUN-01
CHECKED		
APPROVED		
APPROVED		

REFERENCE DOCUMENTS
REF
REF
REF

Scintilla 4901 W. 93rd Av. Apt 2232 Westminster, CO 80031 (303) 857-2859

TITLE: DDX ILLUMINATOR SYSTEM FORTH MECHANICAL ASSEMBLY

SIZE B | TYPE MACH | DWG NO. | REV. 1

SCALE 1/1 | CONTRACT | SHEET 1 OF 1

OPTICAL BENCH. LIGHT RAYS ARE MODELED IN THIS RENDERING. THE LASER IS SHOWN AT THE NOMINAL 13.5° FROM THE TEST PEICE. IT IS ADJUSTABLE FROM 4.5–34.5°. THE LASER AND LENS CELL HOLDERS ARE C–CLAMPS. THEY WILL BE MACHINED SUCH THAT A SET SCREW IS NTO NEEDED, BUT IN THE FUTURE IT MAY BE NEEDED SO THE SET SCREW WILL BE MACHINED NOW (AS SHOWN). THE LENS CELL HAS ADJUSTABILITY VERTICAL TO THE TEST PEICE WITH STRAIGHT PIN–N–SLOT & ONE RETENTION SCREW IN THE SAME MANNER AS THE LASER HAS ROTATIONAL ADJUSTABILITY.

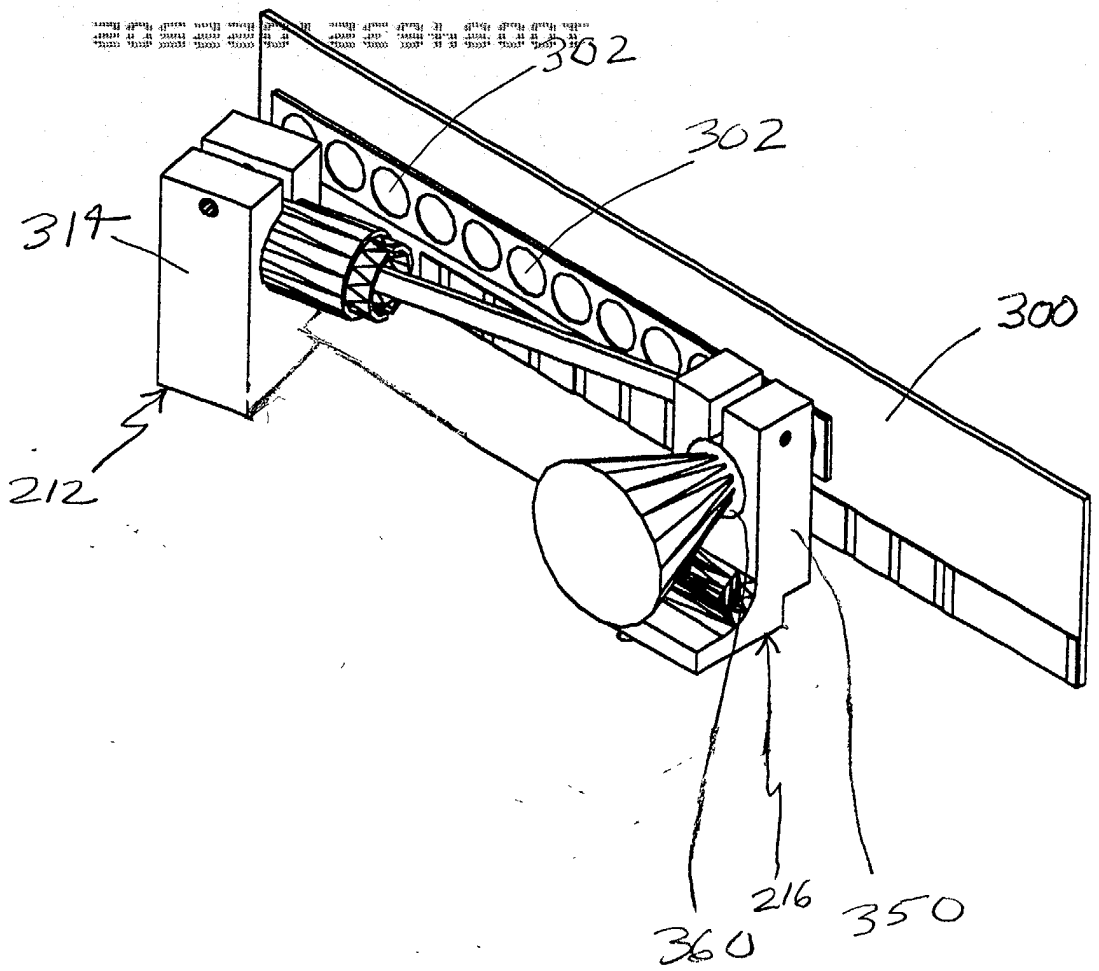
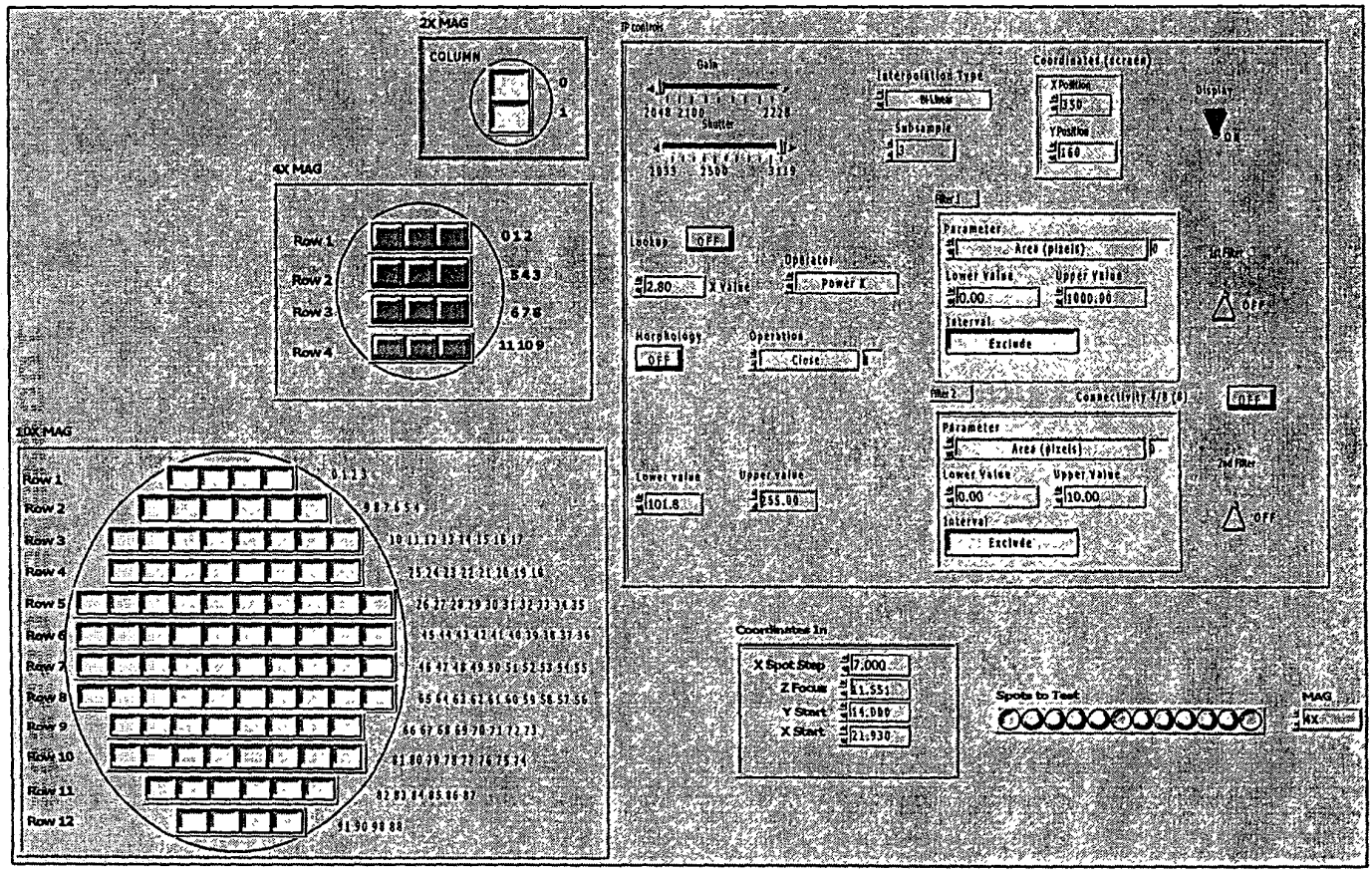


Fig. 20

Write Profile.vi
D:\Data\Projects\AccelR8 DDx Optest\Programming\QuanDx10-28-01.llb\Write Profile.vi
Last modified on 10/29/2001 at 12:59 PM
Printed on 11/15/2001 at 1:09 AM

Front Panel



Controls and Indicators

MAG

2X MAG

COLUMN

Boolean

4X MAG

Row 1

Boolean

Row 2

Boolean

Row 3

Boolean

Row 4

Boolean

10X MAG

Row 1

Fig. 21

Front Panel

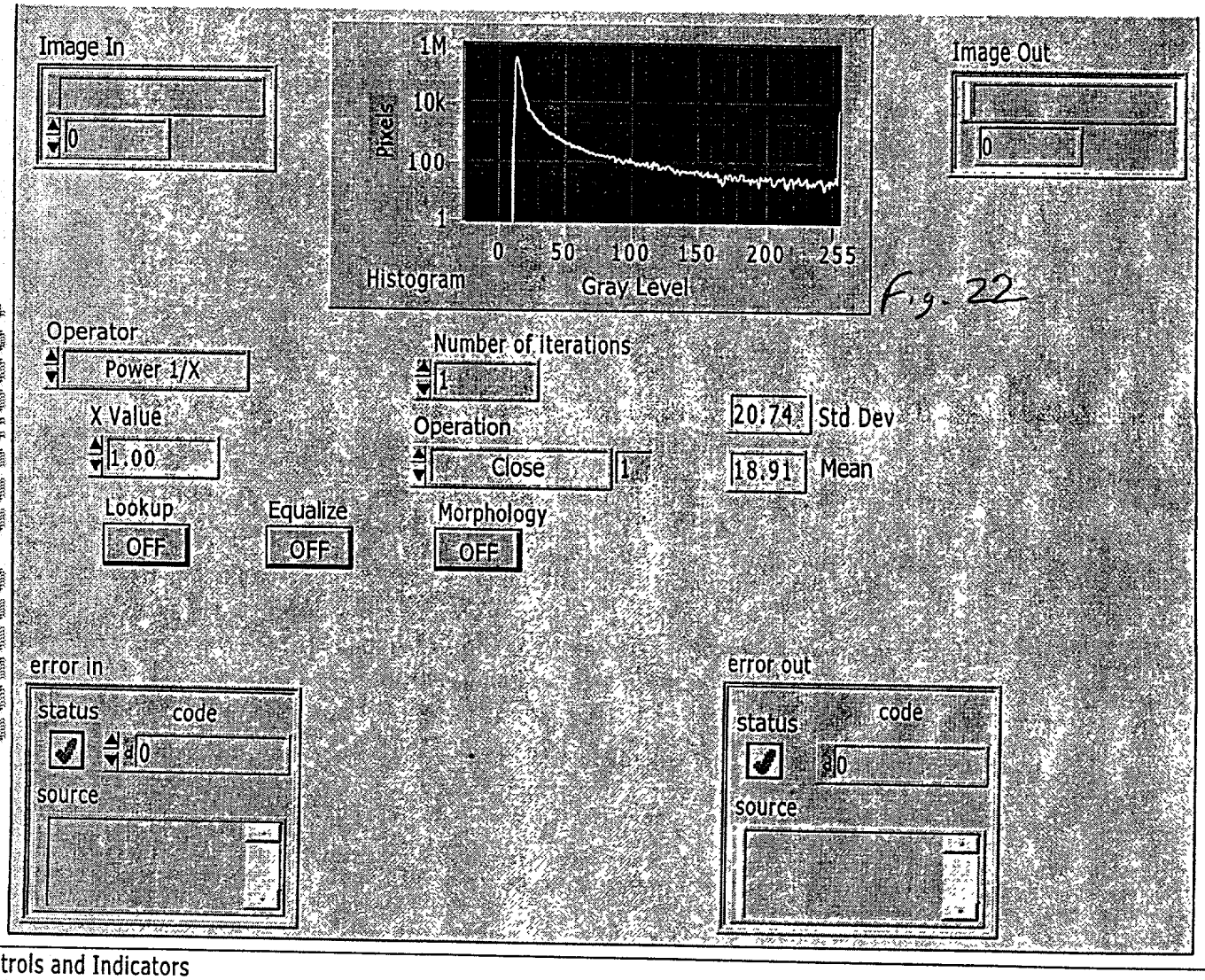


Fig. 22

Controls and Indicators

Operator
Operator specifies the remapping procedure used.

X Value
X Value is a value used only for the operators Power X and Power 1/X.

Equalize

Operation
Operation specifies the type of morphological transformation procedure to use.

Lookup

error in
The <B>error in</B> cluster can accept error information wired from VIs previously called. Use this information to decide if any functionality should be bypassed in the event of errors from other VIs.

The pop-up option <B>Explain Error</B> (or Explain Warning) gives more information about the error displayed.

INSTRUMENT SETUP

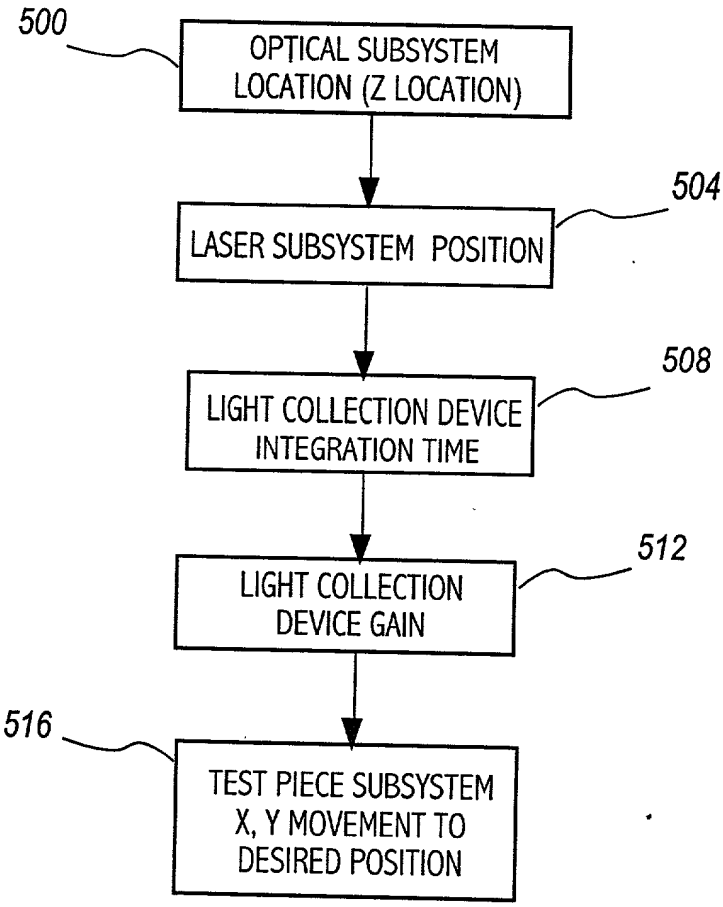


Fig. 23

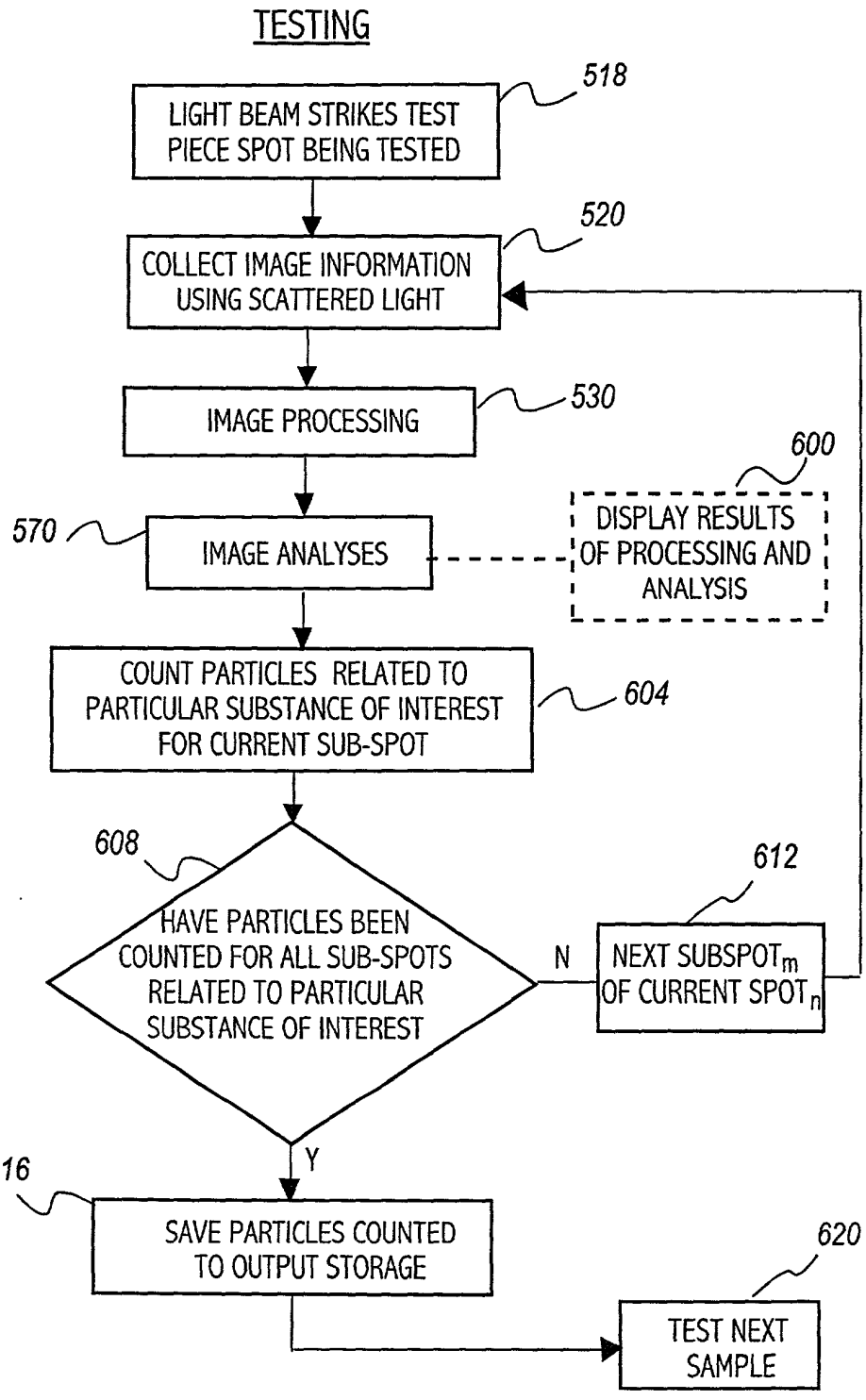

TESTING
518
LIGHT BEAM STRIKES TEST PIECE SPOT BEING TESTED
520
COLLECT IMAGE INFORMATION USING SCATTERED LIGHT
530
IMAGE PROCESSING
600
DISPLAY RESULTS OF PROCESSING AND ANALYSIS
570
IMAGE ANALYSES
604
COUNT PARTICLES RELATED TO PARTICULAR SUBSTANCE OF INTEREST FOR CURRENT SUB-SPOT
608
HAVE PARTICLES BEEN COUNTED FOR ALL SUB-SPOTS RELATED TO PARTICULAR SUBSTANCE OF INTEREST
N
612
NEXT SUBSPOT$_m$ OF CURRENT SPOT$_n$
Y
616
SAVE PARTICLES COUNTED TO OUTPUT STORAGE
620
TEST NEXT SAMPLE

Fig. 24

IMAGE PROCESSING

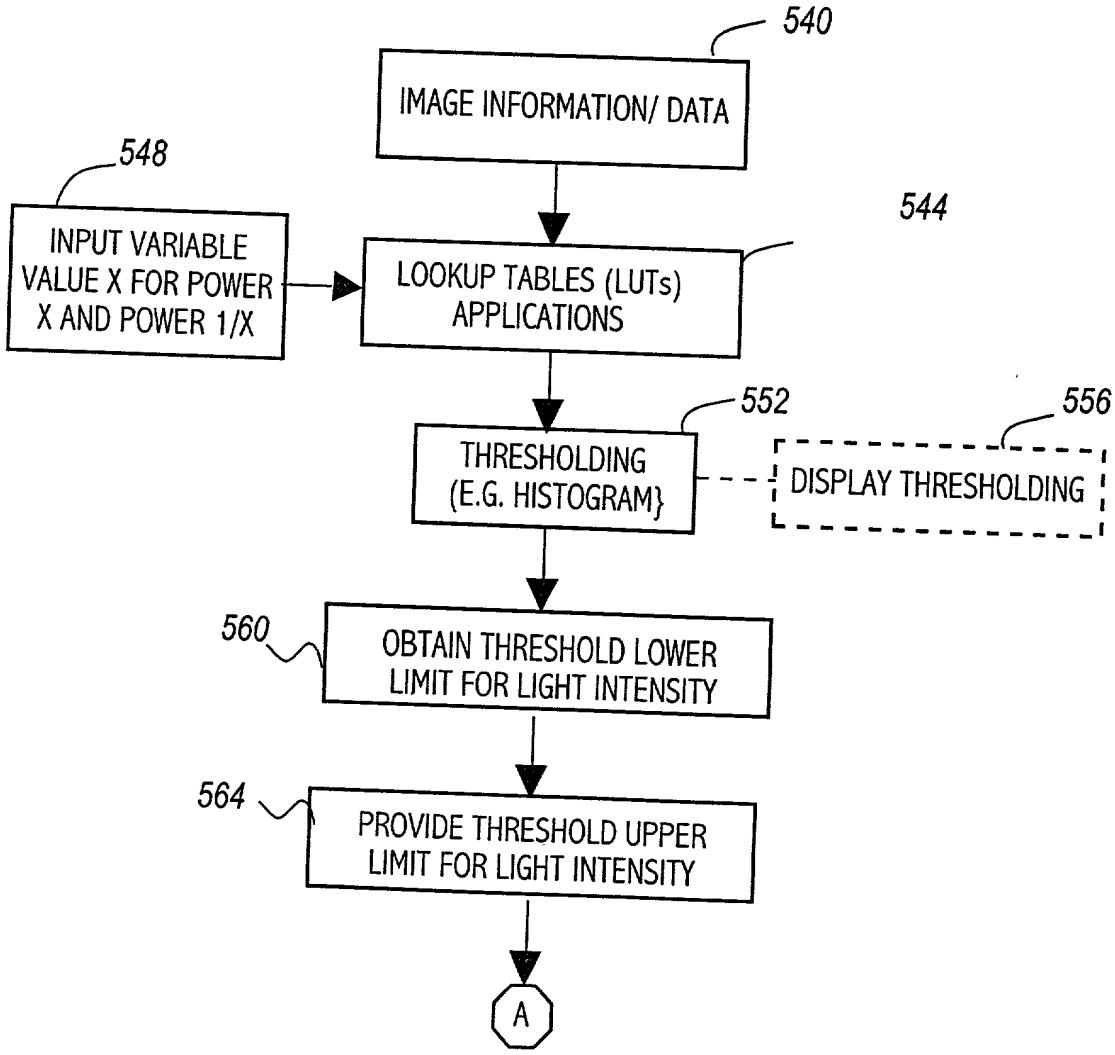


Fig. 25

IMAGE ANALYSIS

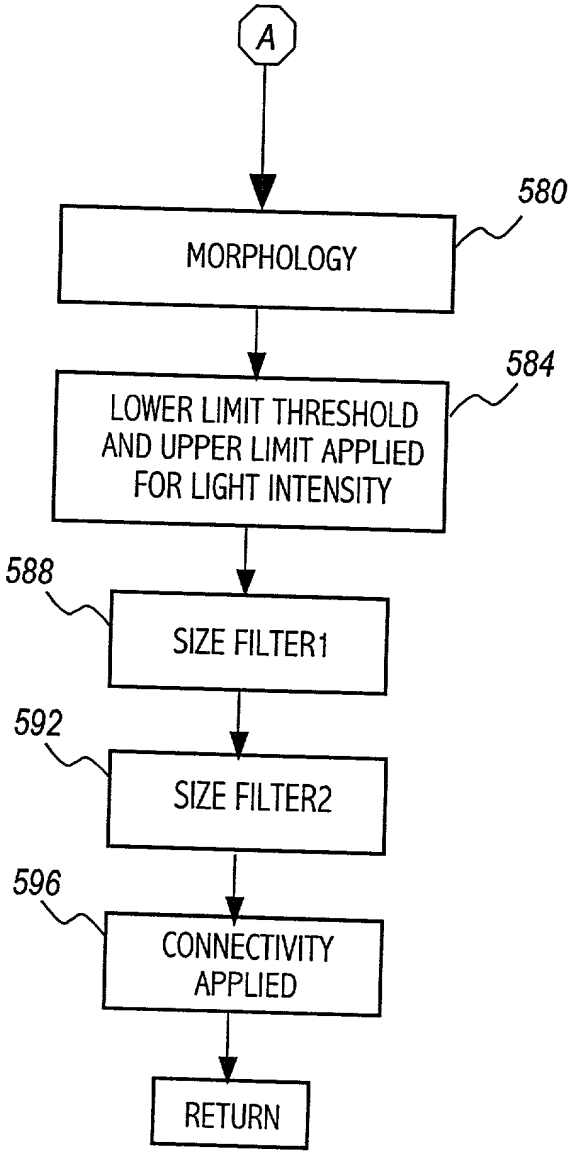


Fig. 26